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# **Livestock network analysis for rhodesiense human African trypanosomiasis control in Uganda**

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## **Abstract**

### ***Background***

Infected cattle sourced from districts with established foci for *T. b. rhodesiense* Human African trypanosomiasis (rHAT) migrating to districts previously unaffected by rHAT have resulted in a significant expansion of the rHAT focus in Uganda. This study explores livestock movement data to describe cattle trade network topology and assess the effects of disease control interventions on the transmission of rHAT infectiousness.

### ***Methods***

Network analysis was used to generate a cattle trade network with livestock data which was collected from cattle traders (n=197) and validated using random graph methods. Additionally, the cattle trade network was combined with a susceptible, infected, recovered (*SIR*) compartmental model to simulate spread of rHAT ( $R_o$  1.287), hence regarded as ‘slow’ pathogen, and evaluate the effects of disease interventions.

### ***Results***

The cattle trade network exhibited low clustering coefficient (0.5) with most cattle markets being weakly connected and a few being highly connected. Also, analysis of the cattle movement data revealed a core group comprising of cattle markets from both eastern (rHAT endemic) and northwest regions (rHAT unaffected area). Presence of a core group may result

in rHAT spread to unaffected districts and occurrence of super spreader cattle market or markets in case of an outbreak. The key cattle markets that may be targeted for routine rHAT surveillance and control included Namutumba, Soroti and Molo all of which were in south east Uganda. Using effective trypanosomiasis such as integrated cattle injection with trypanocides and spraying can sufficiently slow the spread of rHAT in the network.

## **Conclusion**

Cattle trade network analysis indicated a pathway along which *T. b. rhodesiense* could spread northwards from eastern Uganda. Targeted *T. b. rhodesiense* surveillance and control in eastern Uganda, through enhanced public-private partnerships, would serve to limit its spread.

## **Key words**

HAT, cattle market, network analysis, livestock trade, risk, Uganda

## **Introduction**

Animal movements are integral to livestock trade but are not without risk for disease transmission. Infected Indian cattle in transit to Brazil re-introduced rinderpest to Europe in 1920, an infection that was eradicated worldwide in 2011 (1). The Office International des Epizooties (OIE) was established to mitigate risk and combat animal diseases (including zoonoses) at global level (1). That most infectious diseases for humans which are zoonotic in origin only serve to exacerbate risk for humans and animals (2) complicating trade and biosecurity within and between countries. Considerable efforts are put in place, underpinned by government policy to prevent diseases spread, including attempts to develop a One Health approach to protect animal and human health (3). However, despite best efforts, these may be insufficient as evidenced by migration of Africa Rift Valley fever to Madagascar (4) and the struggle faced by Uganda over two decades to halt migration of *T.b. rhodesiense* HAT (rHAT) (5). Public-private partnerships were used to prevent impending epidemic and spread of rHAT in eastern Uganda (6).

Since 2001, movements of infected animals from districts for which rHAT is endemic to new unaffected districts have spread rHAT around the shores of Lake Kyoga, towards the *T.b. gambiense* HAT (gHAT) focus in the north of the country (7, 8, 9, 10). In 2008, 40% of cattle involved in inter-district trade were estimated to have been transported from rHAT endemic zones in the south east to north and central districts (11).

Close examination of livestock movements and market networks offers the opportunity for understanding risk and exploring potential pathogen transmission. Trade is complex and dynamic and can be interrogated using complex network analysis (12,13,14); can accommodate bi-directional relations such as animal movement, trade and contacts (15) and provide a theoretical framework for analysis of network properties and comparisons (16, 17, 18).

Contact network analysis has been used for modelling disease spread and to predict epidemics (19, 20, 21). Social network analysis (SNA) has been used to establish sexual contact relationships for human immunodeficiency virus/acquired immunodeficiency syndrome (22, 23) and has proved useful for studies of infectious disease transmission in livestock and wildlife. Studies include determining spread of tuberculosis in cattle [24] and in brushtail possums [25]; *Escherichia coli* O157 in cattle (26); avian influenza in poultry (27, 28); and Foot and Mouth Disease in the UK (29, 30, 31, 32, 33, 34, 35, 36, 37). Livestock trade networks

have been previously explored using SNA (38, 39, 40) particularly in Africa and in studies linking livestock trade to risk of zoonotic disease spread (41, 42).

This study explores cattle trade dynamics in eastern and northern Uganda regions to 1) understand cattle trade network topology, and 2) evaluate the effects of disease control interventions on the spread of rHAT with varying infectiousness. Specifically, the study aimed to determine the role of the inter and intra district cattle trade in the potential spread of rHAT and identify key cattle markets for targeted disease surveillance and control.

## **Methodology**

### *Study site*

This study was conducted in SE Uganda in Tororo and Namutumba districts. Vegetation cover in the area is mainly composed of savannah grassland interspersed with *Lantana camara* shrubs (43, 44, 45). The study area receives 1200–1500 mm of rainfall annually, which is bimodal in distribution. There are two wet seasons (March–May and September–November) and two dry seasons (December–February and June–August) (43). The daily mean minimum temperature is 15.8C and mean maximum is 27.8C (44). Agricultural economic activity comprises smallholder mixed farming, with over 80% of the population deriving their livelihood from agriculture (43) producing several different food and cash crops and integrate crop production with livestock keeping Revised (46). The main reason for keeping cattle is as draught for crop cultivation; work oxen represent 36.5% to 43.7% of the cattle population (47, 48). Movement of untreated cattle is common in SE Uganda (49). A spatial study showed that predicted spread of endemic vector-borne and parasitic bovine infectious diseases common in these districts include animal African Trypanosomiasis (AAT), theileriosis (East Coast fever), babesiosis, anaplasmosis, heartwater, gastroenteritis, and fascioliasis (50, 51).

Tororo and Namutumba districts have been endemic for rHAT since the late 1980s (52) with human infective parasites identified in indigenous cattle in Tororo district since 1987 (53, 54, 55, 56, 57, 58). *T. b. rhodesiense* HAT has spread around the shores of Lake Kyoga causing significant human outbreaks associated with movement of infected animals (7, 9, 59) driven by a policy of restocking to assist districts further north, impoverished by war and generations of cattle raiding by the Karamajong in the 1980s and 1990s (11). Cattle raiding by the Karamajong depleted the livestock population in some areas to 3% of their original size (60). Although not all districts in eastern and northern Uganda, these regions have similar agro-ecological zones i.e. semi-arid with subsistence farming of cattle, cassava, and millet (61). In Uganda, livestock traders move between districts and are not based within a specific district, thus provide a useful proxy for understanding cattle movement in most regions of Uganda.

### *Sampling and data collection*

Authorized governmental livestock trade (small and large scale) takes place at defined market locations. These are local within districts and operate periodically under the jurisdiction of the local district livestock movement inspectors. All live livestock markets included in this study were identified from the records available at the district veterinary office. Livestock markets were visited on their respective market days and market transaction reports collected. Market transaction reports contained names of the trader and number of animals sold but information on origin and destination was inconsistent. Therefore, information on animal movement was sought from cattle traders. Data was collected both directly (visiting the livestock markets in Tororo and Namutumba districts) and indirectly (livestock markets from other districts which

were not visited but mentioned by the cattle traders). Figure 1 shows the flow of data collection. The livestock markets where data was directly collected has been shown in Figure 2.

Cattle traders, through verbal consent, were interviewed using semi-structured interviews. Questionnaires were designed to capture interviewee information, livestock markets where cattle traders mostly sourced their cattle within the entire livestock trade cycle (annual), the livestock markets that these animals were sold into, and livestock market size. In total, all 197 traders present during the visit were cross-sectionally interviewed in all (n=9) livestock markets in Tororo and Namutumba districts, SE Uganda. The origin and destination of the cattle as collected from this study has been provided (see supplementary material). Apart from collecting network data, we collected information on livestock market, cattle prices, and cattle trade dynamics using direct observation and conducted key informant interviews with local council authorities, cattle traders, and animal health providers.

### *Data analysis*

Social network analysis methods of (62, 63) were applied. Cattle markets represented the nodes (or actors) and the link (or tie) was represented by the connection of cattle markets through movement of cattle. Market attributes were determined by: i) size where big markets (assigned a value of 2) were represented by >20 cattle traders with >100 cattle traded weekly; small markets (assigned a value of 1) were represented by >20 cattle traders with <100 cattle traded weekly, and ii) past studies (secondary data) on *T. b. rhodesiense* prevalence in livestock (11, 64, 65). Data on HAT prevalence in cattle in Uganda was obtained from searching PubMed, EBSCO, parasitology journal databases. The obtained secondary data for *T. b. rhodesiense* prevalence was fitted via beta and uniform distribution and Monte Carlo simulation to obtain 95% uncertainty interval (UI) in R (package = fitdistr) (66). The total value of actor (i.e. cattle market) attribute was weighted by assigning them sizes of the cattle market and prevalence of *T. b. rhodesiense* obtained from the past studies to represent strength of a cattle market (node).

The cattle trade network in Uganda was evaluated by 1) describing the network typology, and 2) identifying key cattle markets (key nodes) that potentially play a major role in disease spread, hence can be a major focus for disease control based on node centrality measures. Network typology was described using inter (network level metrics) and intra (node level metrics) network metrics, and community detection. Inter-network metrics analyzed included the size of the network (total number of cattle markets and contacts that make up the network), density (i.e. measuring the degree of the contacts between pairs of cattle markets in the network), clustering co-efficient (i.e. measuring the average probability of individual cattle markets being directly connected to one another in the network, hence measuring the tendency of the network to cluster), and modularity (measures strength of division of a network into communities, hence used for detecting community structure in a network) using Clauset-Newman-Moore algorithm (62, 67, 68).

Intra-network metrics analyzed included cattle market connectivity (identifying the strong component of the network), centrality (degree of centrality, degree of betweenness and degree of closeness) and cohesiveness (i.e. identifying groups of cattle markets as part of a common structure of contacts such as k-core) (69, 70). The k-core describes the maximal sub-group in which each cattle market has at least degree k. The k is a metric for determining the coreness and therefore help identify tightly interlinked groups within a network. Community detection was done using hierarchical clustering and community membership matrices including block modelling and structural equivalence (71, 72, 73, 74) to identify communities and overlap

between them. Intra and inter network metrics were analyzed in R (package = igraph, package = sna) (75, 76) statistical computing version 3.2.2 (77). Density was computed using the formula in (78). Table 1 provides a summary of the network metrics including their epidemiological significance.

Cattle movement was set as directed (i.e. each cattle market has a direction associated with it) and weighted (i.e. using attributes to assign the importance of the links between cattle markets) since data obtained from livestock traders indicated the flow of cattle. Sensitivity analysis was included by setting cattle movement as undirected i.e. cattle moving to a certain market and coming back to the original market. The study further analyzed clusters (communities) using links rather than nodes (79) within R (package = linkcomm) (80) statistical computing version 3.2.2 (77). By clustering links between the cattle markets, overlapping and nested network structures, key cattle markets that form links across several clusters could be identified (81, 82).

#### *Validation and simulation of disease outbreak and control*

Before conducting disease spread simulation on the network, the network data was first validated using 1) Erdős-Rényi random graphs with binomial distribution, and 2) small world networks via random rewiring (83). Specifically, this involved using observed nodes to generate a random Erdős-Rényi graph and that the observed network exhibited properties of a small world effects i.e. creation of short paths between arbitrary nodes (83). Network validation using random graphs and rewiring recommended in instances where information on the entire network is not available (84).

Using the network typology, the spread of animal disease (using rHAT as an example) was simulated in the network to assess the effects of disease control interventions on disease transmission with varying infectiousness and related probability of transmission ( $\beta$ ). This was achieved by using a stochastic susceptible, infected, recovered (*SIR*) compartmental model. The basic reproductive number ( $R_o$ ) for rHAT was obtained from previous studies (85, 86); average  $R_o$  of 1.287 was used in this study. Given that rHAT  $R_o$  was less than 1.5, it was used to represent a 'slow' pathogen transmission. However, we also simulated a 'fast' ( $R_o$  3) disease transmission to compare with a 'slow' one in the network. Probability of transmitting rHAT along the network ( $\beta$ ) was calculated by dividing rHAT  $R_o$  with its infectious period in livestock which is on average 60 days (two months) (86). The probability of transmission used in this study was 0.02 (1.287 divided by 60) and 30-time steps. In previous studies it has been reported that combination of trypanocide treatment and insecticide spraying is effective reducing rHAT transmission to  $R_o$  0.0075 (87). Therefore, we reduced the  $\beta$  to 0.000125 to simulate rHAT control using effective methods such as trypanocide treatment and insecticide spraying within the network. Assuming the same infectiousness period as rHAT (i.e. 60 days), we simulated disease control of a 'fast' pathogen by reducing infectiousness by 50% (i.e.  $R_o$  1.5 hence  $\beta$  0.05), and a further 25% (i.e.  $R_o$  0.75 hence  $\beta$  0.0125).

## **Results**

### *Characteristics of livestock markets and cattle trade*

Trade at the major markets is the first tier of the livestock trade chain; subsequent tiers of trading buy livestock from fellow livestock traders to sell on as live animals, for slaughter, breeding or for supply of animal traction. At the first tier, livestock are sold and exchanged between different livestock markets within and outside the district of the market but most often in the same region. Subsequent tiers of trade are within the district where the first-tier livestock market is found. Most livestock traders interviewed traded in livestock reported sourcing animals from within their home or adjacent districts and including districts in the Busoga/ Lake

Victoria crescent rHAT focus such as Iganga and Busia (Figure 2). The cattle markets where cattle traders traded most of their cattle were both in eastern and northern regions of Uganda. The districts in eastern Uganda where cattle were mostly traded are shown in Figure 2 and these included Tororo, Namutumba, Soroti, Serere, Iganga, Busia, Manafa, Butaleja, Bukedea, Kumi, Katakwi and Kaberamaido. The northern districts (see Figure 2) included Dokolo, Amolatar, Lira, Oyam, Gulu, Amuru and Adjumani. The mean selling price according to cattle type was as follows; calves, United States dollar (USD) 37.8 (36.1-39.5), untrained young male for plowing, USD 90.3(87.4-92.3), trained young male for plowing, USD 224.2 (182.7-267.2), cow, USD 207.7 (181.6-232.5), and adult male, USD 381 (275.8-495.2).

### *Network and node metrics*

For SNA analysis, 197 traders were cross-sectionally interviewed in all (n=9) livestock markets in Tororo and Namutumba districts, south-east Uganda. The cattle trade network (Figure 3) comprised of 26 cattle markets both in eastern and northern Uganda, 325 dyads (links between two cattle markets) and 197 links (Table 2) for which there were 60 mutual and 137 duplicated links. In addition, there was only one single connected component within the network. Weighted distances were also calculated to examine the length of all the shortest paths from or to the cattle markets in the network. The distance weighted paths for the cattle markets are shown in Figure 4.

Grouping the cattle markets using clusters and the Clauset-Newman-Moore algorithm, network modularity was 0.1. No isolated cattle markets existed in the network. Most cattle markets were weakly connected with a few being highly connected. Overall elementary graphical indices showed density of the graph to be 0.006; dyadic reciprocity to be 1.7; edgewise reciprocity at 1.6 and eigenvector of centralization at 0.3.

The degree centrality score for each cattle market is shown in Table 3. Soroti livestock market in SE Uganda was shown to have the highest number of links and having a centrality score of 55.0, indicating the highest movement of cattle in and out of the district, followed by adjacent livestock markets in Namutumba (54.0) and Molo (51.0). Katakwi, Lira, Pasindi and Kaberamaido showed a moderate flow of cattle in and out of the district. Ngora, Wawulera, Kumi, Bunyiza, Serere, Siwa, Adjumani, Mukuju, Buhonge, Buhangasi, Dokolo and Amuru livestock markets had a relatively low movement of cattle in and out of the district.

The degree of betweenness and closeness and the k-cores are summarized in Table 4. Namutumba had the highest degree betweenness followed by Molo and Soroti respectively. Namutumba was also observed to have the highest degree of closeness followed by Soroti and Molo. The correlation between closeness and betweenness was 0.8. Animal diseases such as rHAT are most likely to pass through Namutumba district i.e. diseases are most likely to come into Namutumba district and easily passed to other districts via the cattle trade network.

Cattle markets with the highest k-cores were Kaberamaido, Lira, Molo, Namutumba, Pasindi and Soroti. The analysis revealed several nesting cores. By limiting the number of k-cores, the members of the 5-core, as a nesting core, were Soroti, Molo, Katakwi, Kaberamaido, Kumi, Lira and Oyam. The 5-core members may potentially be super spreaders of rHAT and are vulnerable to disease incursion. The key cattle market whose removal would disintegrate the network (articulation points) were Soroti, Namutumba and Molo (Figure 5), representing key nodes where routine disease surveillance and control may be targeted to prevent spread of rHAT.

Examination of structural equivalence as shown in Figure 5, revealed that there were four clusters, indicating similarities in the structure of cattle trade for each cluster. As shown in Figure 6, cluster one was comprised of: Bukedea (ID 5), Bunyiza (ID 6), Munyole (ID 18), Dokolo (ID 9), Amolatar (ID 2), Siwa (ID 24), Busaba (ID 7), Adjumani (ID 1), Kawete (ID 13), Buhonge (ID 4), Mukuju (ID 17), Pasindi (ID 22), Wawulera (ID 26), Amuru (ID 3), Serere (ID 23), Butangasi (ID 8), and Gulu (ID 10). Cluster two was comprised of: Molo (ID 16), Namutumba (ID 19). Cluster three was comprised of Soroti (ID 25). Cluster four was comprised of: Kumi (ID 14), Lira (ID 15), Ngora (ID 20), Oyam (ID 21) Kaberamaido (ID 11) and Katakwi (ID 12). Network block modelling, a measure of similarity using nodes, revealed no single block that connected all others. Extraction of link clusters via single hierarchical clustering, as measure of similarity using links, showed 5 clusters in the network with a maximum partition density of 0.42, the largest having 11 nodes. Additionally, there were five link communities in the cattle network as shown in Figure 7.

From the community membership matrix, the most connected cattle markets (connected to five or more communities) were in order of connectedness: Molo > Soroti > Kaberamaido, Namutumba>Katakwi > Dokolo >Amuru >Amolatar > Pasindi (Figure 8). Livestock markets in SE Uganda comprised 66% of the top connected nodes in the cattle trade network. Limiting actor community membership for the top connected cattle markets to those belonging to three or more communities revealed Molo, Soroti, Kaberamaido, Namutumba and Katakwi to be the most connected markets.

### *Sensitivity analysis*

Sensitivity analysis comparing unweighted and undirected and weighted and directed cattle trade network showed some differences in the k-cores and the top connected livestock markets. K-cores for each actor were twice than for those of a directed network. The top connected nodes in the undirected network were Namutumba, Soroti, Kaberamaido, Katakwi, Molo, Amuru, Lira, Pasindi, Kumi, and Ngora. Therefore, in the undirected cattle network, SE Uganda livestock comprised of 78% of the top connected nodes. The articulation points (cut points), which were Namutumba, Molo and Soroti was the same in both directed and undirected networks.

### *Simulated disease transmission*

Starting from a random cattle market, it was simulated that rHAT would have spread to six cattle markets at 30-time step. Using effective rHAT control methods such as combined cattle treatment and spraying would reduce the transmission to only one cattle market (Figure 9). In comparison to a highly infectious pathogen, 20 cattle markets would have been infected at the initial 30-time step (i.e.  $R_0$  0.05) reducing to 12 cattle market when infectiousness was reduced by 50% (i.e.  $R_0$  0.025), and eventually six cattle markets when infectiousness was reduced by a further 25% ( $R_0$  0.0125) (Figure 10).

## **Discussion**

*T. b. rhodesiense* has rapidly spread through the cattle trade network in Uganda, moving infection progressively northwards. Previous work confirmed the contribution of livestock movements through formal livestock markets and restocking in disease spread. Uganda is a



source of meat for the East African community, Democratic Republic of the Congo, and Southern Sudan (11).

Human infective parasites were first observed in indigenous cattle in Tororo district in 1987 (52). *T.b. rhodesiense* HAT rapidly spread around the shores of Lake Kyoga causing significant human outbreaks that were associated with movement of infected animals (7, 9, 58) driven by a policy of restocking districts impoverished by war and generations of cattle raiding by the Karamajong. Restoration of peace in north-west Uganda and South Sudan is a significant driver for the trade and sale of livestock for meat between the two countries (11). Another potential driver of cattle is cattle prices. In this study, we found that cattle prices are influenced by biophysical characteristics and demand for animal traction, with adult male cattle and young male trained for plowing fetching the highest prices. Further analysis of factors underlying livestock movement is still required to be done.

Analysis of livestock movement data has been shown to be valuable mostly in high income countries where such data are routinely collected. In developing countries, data on livestock movement detailing origin, destination, number of cattle sold, cattle prices etc are limited and in most cases unavailable. Equally, resources are not always available to routinely collect and collate such data for decision making. By collecting cattle movement data from cattle traders, this study shows that it is possible to use expert domain knowledge to construct a network. The value of conducting livestock network analysis in resource limited settings, lies in the possibility of identifying key cattle markets that can be targeted for routine disease control, reducing costs and disease impact. Additionally, simulating animal disease spread enhances understanding of the effectiveness of disease control methods. For example, in this study, we show that for 'slow' pathogens like rHAT, effective treatment strategies can sufficiently reduce the spread of rHAT. It has been shown that treatment of cattle using diminazine aceturate and spraying for tsetse flies to protect cattle against trypanosomiasis is effective and with high net benefits (88, 89, 90). Compared to 'slow' pathogens such as rHAT, control of 'fast' pathogens within the network maybe be problematic and costly requiring a wider coverage of cattle markets or a highly effective control method or methods. This is because even when disease infectiousness and transmission is reduced to 25% the number of infected cattle markets was still substantial.

The cattle network examined here can be categorised as both connected and heterogeneous. Heterogeneity coupled with a low clustering coefficient, asymmetry and high skewness as found in this study is typical of scale-free networks (95). The low density (0.3%) and clustering coefficient (0.5) indicate that the cattle trade network has a random pattern making it difficult to predict a future likely source of rHAT. Cattle and poultry trade network studies in Madagascar (4, 41) showed a similar weakly connected network with low density and clustering coefficient. The average centrality value for the cattle trade network in this study was low indicating that cattle are being moved through few connections; most likely, as a result of majority livestock traders in Uganda operating at small scale. While low connection within the trade network raises the probability of low disease detection, it does offer opportunity to control disease spread within the network.

Examination of degree centrality and betweenness, revealed that Soroti had a high cattle movement in and out the district, whereas most cattle passed through Namutumba. Therefore, rHAT and other infectious diseases can easily start at this district or be passed to other districts. Equally, most animal diseases can easily be transferred to Namutumba district and passed to other districts. In the past, Soroti was an epicenter of rHAT outbreak in 1999/2000 which was linked to Brooks Corner livestock market (currently in Serere district) (7).

The study also identified a core group (5-core) of cattle markets that are vulnerable to rHAT and perhaps other animal diseases, and may act as superspreaders. The members of the core group were the most connected markets, with the highest flow (in and out) of cattle, and they were found in eastern and north-west districts of Uganda; increasing the probability of spread of rHAT from endemic south-east to non-endemic northern parts of Uganda. Members of the core group in eastern Uganda included Namutumba, Molo, Soroti, Pasindi, Wawulera, Ngora, Kumi and Katakwi whereas northern Uganda markets included Oyam and Lira. This core group would maintain infection and serve as an epicenter for the spread of infection to other cattle markets in Uganda; particularly if the original infection was from Namutumba, Soroti or Molo livestock markets.

Cattle markets that connect south-east and north-west Uganda play a key role in the spread of pathogens. Consequently, Government policy dictates that cattle sold at markets should be treated with trypanocidal drugs prior to sale to prevent movement of *T. b. rhodesiense* infected cattle. Implementation of this policy however, is not straight forward. It is the responsibility of the purchaser to pay for both the trypanocides (approximately US\$0.30 per animal for treatment with curative diminazene aceturate to US\$ 0.75 each animal for treatment with isometamidium chloride which has a three month prophylactic effect) along with the veterinary fees for administering the treatment (approximately US\$ 0.30 per animal). Most cattle markets are not perimeter secure; resulting in buyers frequently avoiding extra costs by leaving. Another challenge is that animals purchased for subsequent slaughter should not be treated with trypanocides or should only be slaughtered after the withdraw period of such trypanocides. Aside from the requirement to treat cattle in livestock markets, Uganda law also decrees that any animal destined to move across district boundaries has the correct permit for passage between the specified districts. Ideally, permits should be issued by qualified veterinary personnel subject to animals passing an inspection (examination of clinical manifestations of any communicable disease). Permit records should be kept by the District Veterinary Officer's office from the market of issue, with duplicates dispatched to the Ministry of Agriculture Animal Industry and Fisheries, Entebbe. However, implementation of all the required laws is challenging. Therefore, from a practical point view, network analysis can be used to inform risk-based and targeted disease surveillance and control to circumvent some of the challenges in implementing disease control laws.

This study had limitations. First, livestock markets and cattle traders in northern and some parts of eastern Uganda were not interviewed as the study was focussed on rHAT and lacked resources to expand to other parts of the country. This resulted in a relatively smaller sample size which may affect the cattle network metrics. Second, the study relied on past *T. b. rhodesiense* prevalence as an attribute given no blood samples were taken from cattle. Consequently, further research on livestock markets as well as sampling for *T. b. rhodesiense* is recommended. Third, the cattle network does not incorporate dynamic patterns such as seasonality thereby limiting its complexity; longitudinal collection of cattle movement within a set period e.g. one year is required. Further limitation include use of a simple epidemiological model to simulate disease control; sophisticated modelling may make substantial differences in disease transmission more apparent.

This study recommends: i) control through chemotherapy and spraying of cattle with tsetse-effective insecticides and targeted surveillance of rHAT in key cattle markets (nodes) such as Namutumba, Soroti and Molo cattle markets as opposed to untargeted disease control that may be costly, ii) further targeted and routine surveillance in cattle markets in eastern and north-west Uganda to detect the presence of rHAT in cattle, iii) additional collection and analysis of livestock movement data from more cattle markets to understand animal disease risk. Spraying of cattle with deltamethrin using the restricted application protocol in addition to cattle

treatment with curative trypanocides at the point of sale (e.g. in the cattle markets) is recommended by (7, 51). Trypanocidal drugs capable of temporarily clearing cattle of the human infective parasite are well understood and widely available; tsetse-fly targeted insecticides to prevent reinfection of cattle are also well understood and widely available (91, 92, 93, 94, 95, 96, 97, 98, 99). The restricted application approach (RAP) to insecticide use at markets will reduce costs and is practically feasible (100). However, farmers require support for management of disease and policy to treat animals for the prevention of spread of diseases such as trypanosomiasis and tick-borne diseases needs to be reinforced (101, 102). Furthermore, indigenous cattle are predominantly kept under traditional communal grazing management and are either tethered or grazed on communal pastures. Under these management systems, cattle are exposed to continuous tsetse and tick challenge and the new strains of tsetse and tick-borne diseases (trypanosomiasis, anaplasmosis, babesiosis and theileriosis) imported are difficult to contain following their introduction.

## **Conclusion**

*T. b. rhodesiense* can potentially be spread both within south-east and between this region and north-west Uganda by cattle trading. Targeted *T. b. rhodesiense* surveillance in cattle markets in south-east and north-west Uganda would enable early disease detection. Reinforcement of government policy for treatment of cattle at point of sale through trypanocidal treatment and spraying to protect them from reinfection should be prioritised in eastern Uganda to limit spread of infection. The combined impact of these two interventions (i.e. trypanocidal injection and insecticide spraying), through public-private partnerships, will reduce the risk of reinfection caused by cattle moving into rHAT previously affected as well as unaffected regions of Uganda.

## **Declarations**

### **Ethical approval**

This study was reviewed by the Makerere University College of Veterinary Medicine Animal Resources and Biosecurity ethical review board. It was approved by the Uganda National Council for Science and Technology and approved under approval number HS1336.

### **Consent for publication.**

Not applicable.

### **Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author (WOO) on request. All relevant data are included within this paper and its additional files.

### **Competing interests**

The authors declare that they have no competing interests

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### **Authors' contribution**

WOO was responsible for conception, design, collection, drafting and analysis of data. DM/CAA were involved in conception of the study and data collection. AS was involved in conception, design, analysis and drafting the manuscript. SCW and CW were involved in conception of the study, design, and revision of the manuscript. EM was involved in design and drafting of the manuscript. All authors read and approved the final version of the manuscript.

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### **References**

1. Zepeda, C., Salmana, M., Ruppanner, R. (2001). International trade, animal health and veterinary epidemiology: challenges and opportunities. *Prev. Vet. Med.* 48, 261-271.
2. Taylor, L.H., Latham, S.M., Woolhouse, M.E.J. (2001). Risk factors for human disease emergence. *Phil. Trans. R. Soc. Lond.* doi.org/10.1098/rstb.2001.0888
3. Welburn, S. (2011). One Health: the 21 st century challenge. *Vet. Rec.* 168(23), 614-5.
4. Nicolas, G., Durand, B., Duboz, R., Rakotondravao, R., Chevalier V. (2013). Description and analysis of the cattle trade network in the Madagascar highlands: Potential role in the diffusion of Rift Valley fever virus. *Acta. Trop.* 126(1), 19-27.
5. Waiswa, C., Wangoola, M.R. (2019). Sustaining Efforts of Controlling Zoonotic Sleeping Sickness in Uganda Using Trypanocidal Treatment and Spray of Cattle with Deltamethrin. *Vector Borne Zoonotic Dis.* 8, 613-618. doi: 10.1089/vbz.2018.2382.
6. Kabasa, J.D. (2007). Public-private partnership works to stamp out sleeping sickness in Uganda. *Trends Parasitol.* 23(5), 191-192. doi: 10.1016/j.pt.2007.03.006
7. Fèvre, E.M., Coleman, P.G., Odiit, M., Magona, J.W., Welburn, S.C., Woolhouse, M.E. (2001). The origins of a new *Trypanosoma brucei rhodesiense* sleeping sickness outbreak in eastern Uganda. *Lancet.* 358, 625–628.

8. Hutchinson, C., Fèvre, E., Carrington, M., Welburn, S.C. (2003). Farmer went to market: Lessons learnt from the re-emergence of *T. brucei rhodesiense* sleeping sickness in Uganda. *Lancet Infect Dis.* 3(1), 42-5.
9. Picozzi, K., Fèvre, E.M., Odiit, M., Carrington, M., Eisler, M.C., Maudlin, I., Welburn, S.C. (2005). Sleeping sickness in Uganda: a thin line between two fatal diseases. *Br. Med. J.* 331(7527), 1238–1241.
10. Wangoola, E.M., Bardosh, K., Among, A.C., Welburn, S.C., Waiswa, C., Bugeza, J. (2019). Factors associated with persistence of African animal trypanosomiasis in Lango subregion, northern Uganda. *Trop. Anim. Health Prod.* 51, 2011–2018
11. Selby, R., Bardosh, K., Waiswa, C., Welburn, S.C. (2013). Cattle movements and trypanosomes: Restocking efforts and the spread of Rhodesian sleeping sickness in post-conflict Uganda. *Parasit. Vectors.* 6, 281. doi:10.1186/1756-3305-6-281.
12. Danon, L., Ford, A.P., House, T., Jewell, C.P., Keeling, M.J., Roberts, G.O., Ross, J.V., Vernon, M.C. (2011). Networks and the epidemiology of infectious disease. *Interdiscip. Perspect. Infect. Dis.* 284909. [doi.org/10.1155/2011/284909](https://doi.org/10.1155/2011/284909)
13. Strogatz, S.H. (2001). Exploring complex networks. *Nature.* 410, 268-276. doi:10.1038/35065725.
14. Krause, J., Croft, D.P., James, R. (2007). Social network theory in the behavioural sciences: potential applications. *Behav. Ecol. Sociobiol.* 62, 15–27.
15. Martínez-López, B., Perez, A.M., Sánchez-Vizcaíno, J.M. (2009). Social network analysis. Review of general concepts and use in preventive veterinary medicine. *Transbound. Emerg. Dis.* 56(4), 109-20. doi: 10.1111/j.1865-1682.2009.01073.x.
16. Duncan, J.W., Strogatz, S.H. (1998). Collective dynamics of 'small-world' networks. *Nature.* 393, 440-442.
17. Newman, M.E.J, Watts, D.J., Strogatz, S.H. (2000). Random graph models of social networks. *PNAS.* 99(1), 2566–2572.
18. Scott, J. (2013). *Social Network Analysis: A Handbook*. London: Sage Publications. ISBN 978-1-4462-0903-5.
19. Keeling, M.J., Eames, K.T. (2005). Networks and epidemic models. *J. R. Soc. Interface.* 2(4), 295–307.
20. Meyers, L.A., Newman ,M.E.J., Martin, M., Schrag, S. (2003). Applying network theory to epidemics: control measures for *Mycoplasma pneumoniae* outbreaks. *Emerg. Infect. Dis.* 9, 204–210.
21. Meyers, L.A., Pourbohloul, B., Newman, M.E., Skowronski, D.M., Brunham, R.C. (2005). Network theory and SARS: predicting outbreak diversity. *J. Theor. Biol.* 232(1), 71-81.
22. Klov Dahl, A.S. (1985). Social networks and the spread of infectious diseases: the AIDS example. *Soc. Sci. Med.* 21(11), 1203-1216.
23. May, R.M., Anderson, R.M. (1987). Transmission dynamics of HIV infection. *Nature.* 326 (6109), 137–142.
24. Mekonnen, G.A., Conlan, A.J.K., Berg, S., Ayele, B.T., Alemu, A., Guta, S., Lakew, M., Tadesse, B., Gebre, S., Wood, J.L.N., Ameni, G; ETHICOBOTS consortium. (2019). Prevalence of bovine tuberculosis and its associated risk factors in the emerging dairy belts of regional cities in Ethiopia. *Prev. Vet. Med.* 168, 81-89. doi: 10.1016/j.prevetmed.2019.04.010.

25. Corner, L.A.L., Stevenson, M.A., Collins, D.M., Morris, R.S. (2003). The re-emergence of *Mycobacterium bovis* infection in brushtail possums (*Trichosurus vulpecula*) after localised possum eradication. N. Z. Vet. J. 51(2), 73-80. DOI: [10.1080/00480169.2003.36343](https://doi.org/10.1080/00480169.2003.36343)
26. Turner, J., Bowers, R.G., Clancy, D., Behnke, M.C., Christley, R.M. (2008). A network model of *E. coli* O157 transmission within a typical UK dairy herd: the effect of heterogeneity and clustering on the prevalence of infection. J. Theor. Biol. 254, 45–54.
27. Dent, J.E., Kao, R.R., Kiss, I.Z., Hyder, K., Arnold, M. (2008). Contact structures in the poultry industry in Great Britain: exploring transmission routes for a potential avian influenza virus epidemic. BMC Vet. Res. 4, 27. doi:10.1186/1746-6148-4-27
28. Poolkhet, C., Chairatanayuth, P., Thongratsakul, S., Kasemsuwan, S., Rukkwamsuk, T. (2013). Social network analysis used to assess the relationship between the spread of avian influenza and movement patterns of backyard chickens in Ratchaburi. Thailand Res. Vet. Sci. 95(1), 82-86.
29. Christley, R.M., French, N.P. (2003). Small-world topology of UK racing: the potential for rapid spread of infectious agents. Equine Vet. J. 35, 586–589.
30. Christley, R.M., Robinson, S.E., Lysons, R., French, N.P. (2005). Network analysis of cattle movement in Great Britain. Proc. Soc. Vet. Epidemiol. Prev. Med. 234-244.
31. Woolhouse, M.E.J., Shaw D.J., Liu, L., Mellor, D.J., Thomas, M.R. (2005). Epidemiological implications of the contact network structure for cattle farms and the 20–80 rule. Biol. Lett. 1, 350–352.
32. Webb, C.R. (2006). Farm animal networks: unraveling the contact structure of the British sheep population. Prev. Vet. Med. 68, 3–17.
33. Ortiz-Pelaez, A., Pfeiffer, D.U., Soares-Magalhães, R.J., Guitian, F.J. (2006). Use of social network analysis to characterize the pattern of animal movements in the initial phases of the 2001 foot and mouth disease (FMD) epidemic in the UK. Prev. Vet. Med. 76(1-2), 40–55.
34. Robinson, S.E., Christley, R.M. (2007). Exploring the role of auction markets in cattle movements within Great Britain. Prev. Vet. Med. 81(1-3), 21-37.
35. Webb, C.R. (2006). Investigating the potential spread of infectious diseases of sheep via agricultural shows in Great Britain. Epidemiol. Infect. 134, 31-40.
36. Kiss, I.Z., Green, D.M., Kao, R.R. (2006). The network of sheep movements within Great Britain: network properties and their implications for infectious disease spread. J. Roy. Soc. Interface. 3, 669-677.
37. Bigras-Poulin, M., Barfod, K., Mortensen, S., Greiner, M. (2007). Relationship of trade patterns of the Danish swine industry animal movement network to potential disease spread. Prev. Vet. Med. 80, 143–165.
38. Bajardi, P., Barrat, A., Natale, F., Savini, L., Colizza, V. (2010). Dynamical Patterns of Cattle Trade Movements. PLoS ONE. 6(5), e19869. doi:10.1371/journal.pone.0019869.
39. Hardstaff, J.L., Häslér, B., Rushton, J.R. (2015). Livestock trade networks for guiding animal health surveillance. BMC Vet. Res. 11:82. DOI 10.1186/s12917-015-0354-4.
40. Lentz, H.H.K., Koher, A., Hövel, P., Gethmann, J., Sauter-Louis, C., Selhorst, T., et al. (2016). Disease Spread through Animal Movements: A Static and Temporal Network Analysis of Pig Trade in Germany. PLoS ONE. 11(5), e0155196. doi.org/10.1371/journal.pone.0155196

41. Rasamoelina-Andriamanivo H., Dubozc, R., Lancelotd, R., Maminiainaa, O.F., Jourdane, M., Rakotondramaroa, T.M.C., Rakotonjanaharya, S.N., Servan de Almeida, R., Rakotondravaoa, D.B and Chevalierc, V. (2014). Description and analysis of the poultry trading network in the Lake Alaotra region, Madagascar: Implications for the surveillance and control of Newcastle disease. *Acta Trop.*135, 10–18.
42. Motta, P., Porphyre, T., Handel, I., Hamman, S.M., Ngwa, N.V., Tanya, V., et al. (2017). Implications of the cattle trade network in Cameroon for regional disease prevention and control. *Sci Rep.*2017;43932. doi.org/10.1038/srep43932
43. Magona, J.W., Greiner, M., Mehiltz, D. (2000). Impact of tsetse control on the age-specific prevalence of Trypanosomiasis in village cattle in southeast Uganda. *Trop. Anim. Health Prod.* 32(2), 87–98.
44. Okiria, R., Okuna, N.M., Magona, J.W., Mayende, J.S. (2002). Sustainability of tsetse control by subsequent treatment of 10% of a previously treated Ugandan cattle population with 1% w/v deltamethrin. *Trop. Anim. Health Prod.* 34(2), 105-14. doi: 10.1023/a:1014239305328.
45. Magona, J.W., Mayende, J.S., Olaho-Mukani, W., Coleman, P.G., Jonsson, N.N., Welburn, S.C., Eisler, M.C. (2003). A comparative study on the clinical, parasitological and molecular diagnosis of bovine trypanosomosis in Uganda. *Onderstepoort J. Vet. Res.* 70(3), 13-8
46. Okello-Onen, J., Tukahirwa, E.M., Perry, B.D., Rowlands, G.J., Nagda, S.N., Musisi, G., Bode, E., Heinonen, R., Mwayi, W., Opuda-Asibo, J. (2003). The impact of tick control on the productivity of indigenous cattle under ranch conditions in Uganda. *Trop. Anim. Health Prod.* 35(3) 237-47. doi: 10.1023/a:1023395413568.
47. Ocaido, M., Otim, C.P., Okuna, N.M., Erume, J., Ssekitto, C., Wafula, R.Z.O., Kakaire, D., Walubengo, J., Monrad, J. (2005). Socio-economic and livestock disease survey of agro-pastoral communities in Serere county, Soroti district, Uganda. *Livest. Res. Rural Dev.* 17(8);Article #93
48. Okello, W.O., Muhanguzi, D., MacLeod, E.T., Welburn, S.C., Waiswa, C., Shaw, A.P. (2015). Contribution of draught cattle to rural livelihoods in a district of southeastern Uganda endemic for bovine parasitic diseases: an economic evaluation. *Parasit. Vectors.* 8(571).
49. Batchelor, N.A., Atkinson, P.M., Gething, P.W., Picozzi, K., Fèvre, E.M., Kakembo, A.S.L., Welburn, S.C. (2009). Spatial predictions of Rhodesian human African trypanosomiasis (sleeping sickness) prevalence in Kaberamaido and Dokolo, two newly affected districts of Uganda. *PLoS Neg. Trop. Dis.* 3, e563.
50. Eisler, M.C., Magona, J.W., Revie, C.W. (2012). Diagnosis of Cattle Diseases Endemic to Sub-Saharan Africa: Evaluating a Low Cost Decision Support Tool in Use by Veterinary Personnel. *PLoS One.* 7(7), 1–14. doi:[10.1371/journal.pone.0040687](https://doi.org/10.1371/journal.pone.0040687).
51. Muhanguzi, D., Picozzi, K., Hattendorf, J., Thrusfield, M., Welburn, S.C., Kabasa, J.D., et al. (2014). Prevalence and spatial distribution of *Theileria parva* in cattle under crop-livestock farming systems in Tororo District, Eastern Uganda. *Parasit. Vectors.* 7:91. doi:10.1186/1756-3305-7-91.
52. Odiit, M., Coleman, P.G., McDermott, J.J., Fèvre, E.M., Welburn, S.C., Woolhouse, M.E.J. (2004). Spatial and temporal risk factors for the early detection of *Trypanosoma brucei rhodesiense* sleeping sickness patients in Tororo and Busia districts, Uganda. *Trans. R. Soc. Trop. Med. Hyg.* 98(10):569-576.

53. Tietjen, S., Welburn, S.C., Kalunda, M., Kakaire, D., Tietjen, U., Mehlitz, D. (1991). Investigations on the significance of the animal reservoir of rhodesiense sleeping sickness in Uganda. *Trop. Med. Parasitol.* 42, 450.
54. Hide, G., Welburn, S.C., Tait, A., Maudlin, I. (1994). Epidemiological relationships of *Trypanosoma brucei* stocks from South East Uganda: evidence for different population structures in human infective and non-human infective isolates. *Parasitology.* 109, 95-111.
55. Hide, G., Angus, S., Holmes, PH., Maudlin, I., Welburn., S.C. (1998) Comparison of circulating *Trypanosoma brucei* strains in an endemic and an epidemic area of a sickness focus. *Exp. Parasitol.* 89(1), 21-29.
56. Hide, G., Tilley, A., Welburn, S.C., Maudlin, I., Tait, A. (2000). *Trypanosoma brucei*: Identification of trypanosomes with genotypic similarity to human infective isolates in tsetse from a region free of human sleeping sickness. *Exp. Parasitol.* 96, 67-74.
57. Welburn, S.C., Picozzi, K., Fèvre, E.M., Coleman, P.G., Odiit, M., Carrington, M., Maudlin, I. (2001). Identification of human infective trypanosomes in animal reservoir of sleeping sickness in Uganda by means of serum-resistance-associated (*SRA*) gene. *Lancet.* 358, 2017-19.
58. Welburn, S.C., Coleman, P.G., Maudlin, I., Fèvre, E.M., Odiit, M., Eisler, M.C. (2006). Crisis, what crisis? Control of Rhodesian sleeping sickness. *Trends Parasitol.* 22(3), 123-128.
59. Zoller, T., Fèvre, E.M., Welburn, S.C., Odiit, M., Coleman, P.G. (2008). Analysis of risk factors for T. Brucei rhodesiense sleeping sickness within villages in south-east Uganda. *BMC Infect. Dis.* 8(88):1–9. doi:10.1186/1471-2334-8-88.
60. Gyatt, H. (2001). Cattle market causes chaos. *Trends Parasitol.* 17(11).
61. Okonya, J., Syndikus, K., and Kroschel, J. (2013). Farmers' Perception of and Coping Strategies to Climate Change: Evidence From Six Agro-Ecological Zones of Uganda. *J. Agric. Sci.* 5(8). Doi:10.5539/jas.v5n8p252
62. Borgatti, S., Everett, G., Johnson, C. *Analyzing Social Networks*. Thousand Oaks, CA: Sage (2013).
63. Wasserman, S., Faus, K. *Social Network Analysis: Methods and Applications*. Cambridge: Cambridge University Press (1994).
64. Muhanguzi, D., Picozzi, K., Hattendorf, J., Thrusfield, M., Kabasa, J.D., Waiswa, C., Welburn, S.C. (2014). The burden and spatial distribution of bovine African trypanosomes in small holder crop-livestock production systems in Tororo District, south-eastern Uganda. *Parasit. Vectors.* 7, 603.
65. Hamill, L., Picozzi, K., Fyfe, J., von Wisseman, B., Wastling, S., Wardrop, N., Selby, R., Acup, C.A., Bardosh, K., Munhunguzi, D., Kabasa, J.D., Waiswa, C., Welburn, S.C. (2017). Evaluating the impact of targeting livestock for the prevention of human and animal trypanosomiasis, at village level, in districts newly affected with *T. b. rhodesiense* in Uganda. *Infect. Dis. Poverty.* 6(16). DOI: 10.1186/s40249-016-0224-8.
66. Delignette-Muller, M.L., Dutang, C. (2015). fitdistrplus: An R Package for Fitting Distributions. *J. Stat. Softw.* 64(4), 1-34.
67. Friedkin, N.E. (1984). Structural cohesion and equivalence explanations of social homogeneity. *Sociol. Method Res.* 12, 235–261.



68. Marsden, P.V. (1990). Network data and measurement. *Annu. Rev. Sociol.* 16, 435-463.
69. Newman, M.E.J., Girvan, M. (2004). Finding and evaluating community structure in networks. *Phys. Rev.* 69, 026113.
70. Sabidussi, G. (1966). The centrality index of a graph. *Psychometrika.* 31, 581–603.
71. Gould, R.V. (1987). Measures of betweenness in non-symmetric networks. *Soc. Netw.* 9, 277–282.
72. Watts, D.J., Strogatz, S.H. (1998). Collective dynamics of “small-world” networks. *Nature.* 393, 440–442.
73. Koschützki, D., Lehmann, K.A., Peeters, L., Richter, S., Tenfelde-Podehl, D., Zlotowski, O. (2005). “Centrality indices”, in *Network analysis*, ed. U. Brandes, T. Erleback (Berlin: Springer), 16–61.
74. Clauset, A., Moore, C., Newman, M.E.J. (2008), Hierarchical structure and the prediction of missing links in networks. *Nature.* 453, 98–101.
75. Csardi, G., Nepusz, T. (2006). The igraph software package for complex network research. *InterJournal, Complex Systems.* 1695.  
[http://www.interjournal.org/manuscript\\_abstract.php?361100992](http://www.interjournal.org/manuscript_abstract.php?361100992)
76. Butts, C.T. (2008). Social network analysis with sna. *J. Stat. Softw.* 24(6), 1-51.
77. R Development Core Team. (2007). *R: A language and environment for statistical computing*. Vienna: R Foundation for Statistical computing.
78. Luke, D.A. (2015). “The network analysis Five-Number Summary”, in *A user’s guide to network analysis in R*, ed. D.A. Luke (Switzerland: Springer), 11-16. Doi 10.1007/978-3-319-23883-8.
79. Ahn, Y.Y., Bagrow, J.P., Lehmann, S. (2010). Link communities reveal multiscale complexity in networks. *Nature.* 466: 761–764. doi:10.1038/nature09182.
80. Kalinka, A.T., Tomancak, P. (2011). linkcomm: an R package for the generation, visualization, and analysis of link communities in networks of arbitrary size and type. *Bioinformatics.* 7(14), 2011-2012.
81. Palla, G., Imre Derényi, I., Farkas, I., Vicsek, T. (2005). Uncovering the overlapping community structure of complex networks in nature and society. *Nature.* 435:814-818. doi:10.1038/nature03607.
82. Evans, T.S., Lambiotte, R. (2009). Line graphs, link partitions and overlapping communities. *Phys. Rev. E.* 80, 016105.
83. Watts, D., Strogatz, S. (1998). Collective dynamics of ‘small-world’ networks. *Nature* 393, 440–442 <https://doi.org/10.1038/30918>
84. Bliss, C. A., Danforth, C. M., Dodds, P. S. (2014). Estimation of global network statistics from incomplete data. *PloS one*, 9(10), e108471.  
<https://doi.org/10.1371/journal.pone.0108471>
85. Rogers, D. (1988). A general model for the African trypanosomiasis. *Parasitol.* 97, 193–212
86. Davis, S., Aksoy, S. and Galvani, A. (2011). A global sensitivity analysis for African sleeping sickness. *Parasitol.* 138(4), 516–526. <https://doi.org/10.1017/S0031182010001496>

87. Gervas, H.E., Opoku, N.K.O., Ibrahim, S. (2018). Mathematical modelling of human African trypanosomiasis using control measures. *Comput Math Method M.* 2018, 1-13. <https://doi.org/10.1155/2018/5293568>
88. Muhanguzi, D., Picozzi, K., Hattendorf, J., Thrusfield, M., Welburn, S.C., Kabasa, J.D., et al. (2014). Collateral benefits of restricted insecticide application for control of African trypanosomiasis on *Theileria parva* in cattle: a randomized controlled trial. *Parasit Vectors.* 7:432. doi: 10.1186/1756-3305-7-432
89. Kajunguri, D., Hargrove, J.W., Ouifki, R., Mugisha, J.Y., Coleman, P.G., Welburn, S.C. (2014). Modelling the use of insecticide-treated cattle to control tsetse and *Trypanosoma brucei rhodesiense* in a multi-host population. *Bull Math Biol.* 76, 673–696. doi: 10.1007/s11538-014-9938-6
90. Okello, W.O., MacLeod, E.T., Muhanguzi, D., Waiswa, C., Welburn, S.C. Controlling Tsetse Flies and Ticks Using Insecticide Treatment of Cattle in Tororo District Uganda: Cost Benefit Analysis. *Front. Vet. Sci.* 8, 174. DOI.10.3389/fvets.2021.616865
91. Geerts, S., Holmes, P.H.(1998). Drug management and parasite resistance in bovine trypanosomiasis in Africa. <http://www.fao.org/3/W9791EN/w9791en.pdf>.  
[Accessed 22 September 2020]
92. Holmes, P.H., Eisler, M.C., Geerts. S. (2004). “Current chemotherapy of animal trypanosomiasis”, in *The Trypanosomiasis*, ed I. Maudlin, P.H. Holmes PH, M.A. Miles (Oxfordshire: CAB International).
93. Welburn, S.C., Maudlin, I. (2012). Priorities for the elimination of sleeping sickness. *Adv. Parasitol.* 79, 299-337. doi: 10.1016/B978-0-12-398457-9.00004-4.
94. Babokhov, P., Sanyaolu, A.O., Oyibo, W.A., Fagbenro-Beyioku, A.F., Iriemenam, N.C. (2013). A current analysis of chemotherapy strategies for the treatment of human African trypanosomiasis. *Pathog. Glob. Health.* 107(5), 242-252. doi:10.1179/2047773213Y.00000000105
95. Allsopp, R., Hursey, B.H. (2004). “Insecticidal control of tsetse.” in *The Trypanosomiasis*, ed I. Maudlin, P.H. Holmes PH, M.A. Miles (Oxfordshire: CAB International), 491–507.
96. Hargrove, J.W., Omolo, S., Msalilwa, J.S.I., Fox, B. (2000). Insecticide-treated cattle for tsetse control: the power and the problems. *Med. Vet. Entomol.* 14, 123–130.
97. Torr, S.J, Maudlin, I. (2007). Less is more: restricted application of insecticide to cattle to improve the cost and efficacy of tsetse control. *Med. Vet. Entomol.* 21(4), 53-67.
98. Vale, G.A., Mutika, G., Lovemore, D.F. (1999). Insecticide-treated cattle for controlling tsetse (Diptera: Glossinidae): some questions answered, many posed. *Bull. Entomol. Res.* 89, 567–577.
99. Vale, G.A. and Grant, I.F. (2002). Modelled impact of insecticide-contaminated dung on the abundance and distribution of dung fauna. *Bull. Entomol. Res.* 92, 251–263.
100. Muhanguzi, D., Okello, W.O., Kabasa, J.D., Waiswa, C., Welburn, S.C., Shaw, A.P.M. (2015). Cost analysis of options for management of African animal trypanosomiasis using

interventions targeted at cattle in Tororo District; south-eastern Uganda. *Parasit. Vectors.* 8, 387.

101. Machila, N., Wanyangu, S.W., McDermott, J.J., Welburn, S.C., Maudlin, I. and Eisler, M.C. (2003). Cattle owners perceptions of African Bovine trypanosomiasis and its control in Busia and Kwale Districts of Kenya. *Acta Trop.* 86(1), 25-34.

102. Machila, N., Emongor, R., Shaw, A.P., Welburn, S.C., McDermott, J.J., Maudlin, I., Eisler, M.C. (2007). A community education intervention to improve bovine trypanosomiasis knowledge and appropriate use of trypanocidal drugs on smallholder farms in Kenya. *Agric. Syst.* 94(2), 261-272.

**Table 1: Description of network and node level metrics**

<b>Metric</b>	<b>Description</b>	<b>Epidemiological importance</b>
<b>Network-level metrics</b>		
Size	Number of cattle markets (nodes) that make up the network. It enables comparison of the Uganda cattle market with other markets random graphs.	Larger networks may have more subgroups that act as disease transmission bottlenecks within the group
Density	Degree of contact between pairs of cattle markets in the network	Disease transmission may occur faster in high density networks
Eigenvector centralization	Measures the level of influence of a cattle market (node) within a network after assigning each a score.	Disease transmission occurs rapidly in networks with high eigenvector centralization
Modularity	Involves partitioning of the cattle network into well connected sub-groups	Disease transmission is slowed down by the presence of sub-groups
Clustering coefficient	Is the ratio of the number of edges (i.e. links) that occur between a cattle market's (i.e. node's) immediate neighbors and the maximum number of edges that could exist between them	High clustering may increase the frequency of disease spread
<b>Node level metrics</b>		
Degree centrality	The number of edges (links) a cattle market (node) has.	Indicates whether a cattle market can be source of infection (high out-degree centrality) or receive most of the infection from other cattle markets (high in-degree centrality)
Degree betweenness	Measures the extent to which a cattle market (node) lies on the paths between other cattle markets	Measures the how frequently a given cattle market (node) can act as a bridge between other cattle markets (nodes) in the network. The higher the degree betweenness, the higher the potential of a cattle market to transmit the infection from a source cattle market

K-core	The k-core of a graph is the maximal subgraph made of nodes with degree k or more.	Can identify super spreaders or groups within a network which are vulnerable to a disease
<b>Key actors</b>		
Articulation point	Is a cattle market (node) whose removal disconnects the network	Can be targeted for disease control to enhance the resilience of the network

**Table 2: Cattle trade network metrics in south-east and north-west Uganda.**

Metric	Values	Minimum	Maximum
Number of cattle markets (nodes)	26.0	-	-
Number of links between cattle markets	197.0	-	-
Number of links between two cattle markets (dyads)	325.0	-	-
Density	0.0	-	-
Clustering coefficient	0.5	1.0	0.0
Average degree centrality	5.9	19.0	1.0
Average betweenness centrality	10.8	100.0	0.0
Average closeness centrality	0.0	-	-
Eigenvector centralization	0.3	-	-

**Table 3: Cattle trade network metrics for all markets**

Cattle market ID	Cattle market	Degree centrality	Betweenness centrality	Closeness centrality	K-cores
1	Adjumani	6	0	0	6
2	Amolatar	4	20	0	4
3	Amuru	5	21	0	4
4	Buhonge	3	0	0	3
5	Bukedea	4	0	0	4
6	Bunyiza	9	0	0	8
7	Busaba	1	0	0	1
8	Butangasi	5	0	0	5
9	Dokolo	5	0	0	4
10	Gulu	8	2	0	8
11	Kaberaido	27	16	0	19
12	Katakwi	33	29	0	17
13	Kawete	2	0	0	2
14	Kumi	11	0	0	10
15	Lira	32	9	0	19
16	Molo	51	118	0	19
17	Mukuju	2	0	0	2
18	Munyole	1	0	0	1
19	Namutumba	54	153	0	19
20	Ngora	17	0	0	15
21	Oyam	5	0	0	5
22	Pasindi	30	3	0	19
23	Serere	8	0	0	8
24	Siwa	7	1	0	7
25	Soroti	55	134	0	19
26	Wawulera	13	0	0	13

**Figure 1: Cattle movement data collection and analysis methods**

**Figure 2: Districts in Uganda where cattle are mostly traded. The yellow districts (Namutumba and Tororo) are where data was collected from. Water bodies are shown in blue.**

**Figure 3: Cattle trade network in northern (green nodes) and eastern (blue nodes) Uganda.**

**Figure 4: Weighted distance paths of the cattle trade network**

**Figure 5: Cattle markets where *T. b. rhodesiense* is likely to be spread from. Soroti, Namutumba and Molo shown by green dots.**

**Figure 6: Cattle market structural equivalence within the network.**

**Numbers represent cattle market identification (ID) and red boxes indicate the cluster.**

**Figure 7: Visualization of link communities within the cattle network (using node pies). The fraction of the total number of edges that a node has in each community is depicted using a pie chart**

**Figure 8: Community membership of the top (most) connected cattle markets in south-east and north-west. Colors indicate the community-specific membership and the N-Ary summation ( $\sum$ ) shows the total number of cattle markets in each community.**

**Figure 9: Effect of controlling rHAT when using effective control methods after 30-time steps. Infected nodes are shown in red and uninfected in blue.**

**Figure 10: Effect of controlling 'fast' pathogen ( $R_0$  3) when infectiousness is reduced to 25% ( $R_0$  0.75) after 30-time steps. Infected nodes are shown in red and uninfected in blue.**